

\$4 Million For Unsought NIH Study

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The National Institutes of Health, one of the few agencies on which Capitol Hill regularly showers more money than it requests, may get \$4 million it did not seek this year for a heart drug study it did not recommend.

The drug is Atromid-S, which tends to lower the level of cholesterol and other fatty substances in the bloodstream. The special study is designed to see whether the drug tends to prevent heart attacks.

Sen. Lister Hill (D-Ala.) was so impressed by testimonials on the new drug's prospects that he dropped the \$4 million into the NIH money bill at the last minute without bothering to get the views of the agency that would spend it—NIH's National Heart Institute.

The Atromid-S story illustrates the informality and warm generosity with which

See ATROMID, A5, Col. 1

NIH Is Given \$4 Million For Study It Didn't Seek

the Congressional appropriation process for medical research is sometimes carried out. It also depicts the influence exerted on NIH appropriations by philanthropist Mary Lasker, famed heart surgeon Michael E. de Baakey and others dedicated to generous outlays for biomedical research.

A key date in the story was last April 27, when the Senate Appropriations health subcommittee, headed by Hill, met to hear the fiscal 1968 budget requests of NIH.

A key witness was Dr. Donald S. Frederickson, director of the National Heart Institute — part of the NIH research family. Frederickson mentioned an already established study being conducted at the Heart Institute on five coronary drugs — including Atromid-S.

No one at the hearing questioned Frederickson's assurance that the broad study, known as the Cooperative Drug Study, was "progressing smoothly." No one so much as hinted at a need for a separate project to test Atromid-S.

The existing study is expected to cost up to \$40 million over its ten-year life. The newly proposed special inquiry into Atromid-S would be \$48.6 million over a five-year period.

Had Been Considered

Actually the Heart Institute had considered a separate Atromid-S project. But the cost and inefficiency of such a study, Heart Institute officials concluded, outweighed the "pro" argument that the drug had unusual promise because it might produce fewer and less serious side-effects than other cholesterol-lowering drugs.

Underlying all of this were still — unanswered questions about lowered blood cholesterol levels and the prevention of coronary disease.

The restraint felt in the Institute about requesting a large appropriation for an iffy special project on Atromid-S was not shared by three researchers in California.

Close Friendship

One of these was Dr. Jessie Marmorston, a clinical professor of medicine at the University of California, who acknowledged that she has developed close friendship with Sen. Hill and Mrs. Lasker growing out of their common interest in biomedical research. She said in an interview that she has probably received more Heart Institute funds than any other single investigator.

Dr. Marmorston has performed extensive research on Premarin, a drug that was also included in the Institute's Cooperative Drug Study. Her work on Premarin was criticized in a March, 1961 issue of the Medical Letter, a leading drug-review publication for doctors. It described as "questionable" published claims by Dr. Marmorston of Premarin's life-prolonging qualities in heart attack victims.

Premarin is manufactured

by the makers of Atromid-S—the Ayerst Laboratories division of the American Home Products Corp.

After the FDA approved Atromid-S for sale earlier this year Dr. Marmorston and Dr. de Baakey conferred in Britain with doctors who investigated it there.

Important Roles

The second of the three researchers was John M. Weiner, a statistician associate of Dr. Marmorston who designs clinical experiments.

The third was Dr. Louis R. Krasno. Since November, 1964, he has been testing Atromid-S with 1200 male employees of United Air Lines in San Francisco who have suffered heart attacks. They were matched against an equal number of comparable patients who were not given the drug.

The three Californians and Dr. de Baakey, who has been mentioned as a possible successor to Dr. James A. Shannon as head of the National Institutes, all had important roles in a second Senate Appropriations subcommittee hearing last June 6.

They appeared as citizen-witnesses—a concept adopted about 15 years ago at the urging of Mrs. Lasker. She saw it as a device that might win larger appropriations for the Institutes than Congress would grant if only their officials could appear.

The list of citizen-witnesses is prepared by Mike Gorman, executive director of the National Committee Against Mental Illness and a self-described "over-all bird-dog" for Hill. But, he told a reporter, he merely passes along the list of citizen-witnesses for the Heart Institute; the actual selection is made by Dr. de Baakey.

Shared Friendship

One selection was statistician Weiner, who was proposed by Dr. Marmorston in Los Angeles. Dr. de Baakey's approval was assured. He and Dr. Marmorston shared a belief that Atromid-S had extraordinary promise. They also shared the friendship and trust of Mrs. Lasker, Sen. Hill and the late Rep. John E. Fogarty (D-R.I.), Hill's counterpart in the House.

Hill was the only Senator present to hear Dr. de Baakey, Dr. Krasno, Weiner and two other citizen-witnesses for the Heart Institute.

Dr. de Baakey led off with an impassioned plea for more research funds. Each year, he emphasized, cardiovascular disease causes the deaths of more than 1 million Americans.

The idea of a separate Atromid-S was broached by Dr. Krasno.

He said his studies with the drug, which have not been published, showed three times as many heart attacks in previous victims who did not receive the drug as in those who did. But he cautioned that whether Atromid-S prevents heart attacks—"the most important consideration"—is at

this point an unanswered question. "I make no claim," he said.

Special Project

Weiner then unveiled his proposal for the special Atromid-S project. The participants would number 16,000—almost twice as many as are planned for the Institute's five-drug study. Of the 16,000, half would be women; no women are in the Cooperative Drug Study. Half the women and half the men would be persons who have never had heart attacks—would Atromid-S prevent them? Other participants would be studied to see if the drug would prevent a second or a third heart attack.

In an interview later, Hill made it clear that the proposal impressed him. At the hearing, he asked no questions about the soundness of the experimental design (which is questioned in the Heart Institute), about the cost estimates (which are considered low in the Institute) or about any other significant aspect.

No NIH Reaction

Nor did Hill check to see what reaction the Heart Institute might have. This elicited reactions of surprise in the interviews with Dr. de Baakey who had testified that he and his fellow citizen-witnesses were appearing before the subcommittee "particularly . . . on behalf of the National Heart Institute," and with Dr. Marmorston and Weiner.

They assumed, they later said, that "someone" must have known about the proposal. Yet the Institute's director, Dr. Frederickson did not know what was proposed until long afterward, when a transcript of the closed hearing was published.

Asked about all of this, Hill said that checks with the Institutes are made "sometimes." The clerk of his Appropriations health subcommittee, Herman E. Downey, was blunt. "Most of this stuff that we do, we don't consult with NIH," he said.

Following the June 6 hearing, Hill recommended a reduced starter appropriation of \$4 million for the Atromid-S project. He said it was approved without opposition by the subcommittee, the full committee and the Senate.

When the original committee "print" of the appropriations bill was published, however, it made no reference to the Atromid-S project.

Downey said that the \$4 million seed-money item was "omitted by me by inadvertence." In any case, Hill said, he wanted the item in the bill — and it was included in the final committee report published 24 hours later, on Aug. 1.

Whether the \$4 million—or anything — actually will be appropriated for Atromid-S is uncertain. One reason is that with the death of Rep. Fogarty the House Appropriations health subcommittee has shown signs of taking a more critical look at funding of the National Institutes.